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The mode of action of immunological adjuvants.

Allison AC.

Dawa Corporation, Belmont, CA, USA.

Adjuvants augment immune responses to antigens and influence the balance between cell-mediated and humoral responses, as well as the isotypes of antibodies formed. New adjuvant formulations include antigen-carrying vehicles and small molecules with immunomodulating activity. Widely used two-phase vehicles comprise liposomes and microfluidized squalene or squalene emulsions. These are believed to target antigens to antigen-presenting cells, including dendritic cells (DC), follicular dendritic cells (FDC) and B-lymphocytes. Activation of complement generates C3d, which binds CR2 (CD21) on FDC and B-lymphocytes, thereby stimulating the proliferation of the latter and the generation of B-memory. Targeting of antigens to DC may favour cell-mediated immunity. Immunomodulating agents induce the production of cytokine cascades. In a primary cascade at injection sites TNF-alpha, GM-CSF and IL-1 are produced. TNF-alpha promotes migration of DC to lymphoid tissues, while GM-CSF and IL-1 accelerate the maturation of DC into efficient antigen-presenting cells for T-lymphocytes. In a secondary cytokine cascade in draining lymph nodes, DC produce IL-12, which induces Th1 responses with the production of IFN-gamma. The cytokines elicit cell-mediated immune responses and the formation of antibodies of protective isotypes, such as IgG2a in the mouse and IgG1 in humans. Antibodies of these isotypes activate complement and collaborate with antibody-dependent effector cells in protective immune responses.

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